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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,257	12/21/2001	Peter Krulevitch	IL-10580	6642

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EXAMINER	
BEISNER, WILLIAM H	

ART UNIT	PAPER NUMBER
1744	

DATE MAILED: 10/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,257	KRULEVITCH ET AL.	
	Examiner	Art Unit	
	William H. Beisner	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 16-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/18/2005 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-5 and 16-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claims 1 and 16 employ the transitional language "consisting of". Use of this language excludes any element not specified in the claim. As a result, the metes and bounds of the claims cannot be clearly determined for the following reasons: Currently the claims recite the claimed device in terms of "chambers" rather than structural elements. Does this mean that the claimed device is limited only to a device of "chambers"? In view of the instant specification, these "chambers" are associated with specific structural elements that define these chambers. It is not clear how one looking at the instant claims could clearly determine the metes

and bounds of the claim since, for example, "a PCR reaction chamber" could include a number of structural elements including temperature control devices and detectors. If applicants intend to limit their invention by use of the language "consisting of", it is requested that the claims recite specific structural elements that define a device that is capable of functioning as recited in the preamble of the claim "A microfabricated biopsy and genetic analysis instrument". Note the instant specification indicates that the device can include structure for lysing the sample and filters which are also disclosed in the prior art. Are applicants attempting to claim a device that is capable of performing PCR on a tissue sample that does not include lysing and/or filtering? The instant claims are totally devoid of such structures which are clearly required by the prior art when processing a sample that includes cells or tissues. Clarification and/or correction is requested.

Claims 1 and 16, "said biopsy region" lacks antecedent basis.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-5 and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pourahmadi et al.(WO 99/33559) in view of Krulevitch et al.(US 5,985,217 or US 6,319,474).

With respect to claim 1, the reference of Pourahmadi et al. discloses a microfabricated biopsy and genetic analysis instrument that includes a cutter section and specimen chamber (103) located below the cutter section. See page 20, line 27, to page 21, line 10, which discloses that the opening of the specimen chamber (sample port, 103) can include a mesh that slices a tissue specimen. The instrument includes a specimen treatment section (including treatment chambers 107, 119, 122, 141) located adjacent the specimen chamber (103) and a PCR reaction chamber section that is integral or abuts the specimen treatment section. See page 12, lines 13-26, which discloses that the PCR reaction chamber (143) can be integral or separable relative to the sample treatment section of the instrument.

While the reference of Pourahmadi et al. discloses the use of mesh member for cutting or slicing a tissue sample, instant claim 1 differs by reciting that the cutter includes a tapered opening with a sharp edge for cutting the tissue.

The reference of Krulevitch et al. discloses that it is conventional in the art to integrate a tissue cutting structure into a microfluidic device. The device includes a first member (31) that includes a tapered opening with a cutting edge (35) with atomic sharpness. The cutting member or edge is provided over specimen receiving chamber (34). The reference also discloses that microchannels (40) for processing fluids can be provided in communication with the specimen receiving chamber (34). The microchannels are provided on a separate member (32) bonded to the first member.

In view of this disclosure, it would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the mesh structure of the primary reference with the cutting device taught by the reference of Krulevitch et al. for the known and expected result of providing an alternative means recognized in the art to achieve the same result, cutting or slicing a tissue sample prior to introduction into a microfluidic device. The cutting device suggested by Krulevitch et al. would provide thinner samples than that of the primary reference, thus reducing the time to further process the tissue sample once within the microfluidic device.

With respect to the use of the consisting language, provision of a device that is devoid of reagents and/or controllers, would have been obvious when providing a disposable device wherein the control devices can be reused with other devices. Also, based merely on the source of the sample to be detected and/or the reagents employed, whether or not the system includes a dna purification zone would have been well within the purview of one having ordinary skill in

the art. Furthermore, the presence of purification sections and other sample processing zones can fall within the claimed "specimen treatment and analysis chamber".

With respect to claim 2, the reference of Krulevitch et al. discloses that the cutting edge (35) has a smooth edge with atomic sharpness capable of cutting very thin specimens of tissue.

With respect to claim 3, the reference of Krulevitch et al. discloses that the cutter is constructed of silicon.

With respect to claims 4 and 5, the reference of Pourahmadi et al. discloses the use of microchannels (See Figure 2) to connect the sample chamber (103) with the PCR reaction chamber (143). Also the reference discloses the use of planar members, including glass, to form the device (See page 26, line 35, to page 27, line 28). The reference of Krulevitch et al. disclose construction of the microchannel device of silicon and glass substrates (See column 3, lines 1-12 of Krulevitch et al.).

With respect to claim 16, the PCR reaction chamber is capable of receiving a fluid or sample from the specimen treatment section. Also, the reference of Krulevitch et al. discloses that the use of an additional inlet (45) and microchannel (40) for introduction of processing fluids is known in the art and would have been obvious for the known and expected result of providing additional fluids for processing the tissue slice prior to the cellular processing already discussed by the primary reference of Pourahmadi et al. Finally, the reference of Krulevitch et al. also discloses that it is known to optically view the tissue slice within the receiving chamber/channel (40) (See Figure 3C). In view of this additional disclosure, it would have been obvious to one of ordinary skill in the art to further modify the primary reference of Pourahmadi et al. to include an optical analysis device as suggested by Krulevitch et al. for the known and

expected result of providing an art recognized means for optically analyzing the tissue slice prior to further processing within the microfluidic device.

With respect to claim 17, the reference of Pourahmadi et al. discloses that the PCR reaction section (143) can be formed as a separate member or integral member (See page 12, lines 14-16).

With respect to claim 18, the reference of Pourahmadi et al. discloses that the PCR reaction chamber (143) includes a heater (See page 12, lines 13-26) and the reference of Krulevitch et al. discloses that the cutting edge (35) has a smooth edge with atomic sharpness capable of cutting very thin specimens of tissue.

With respect to claim 19, the reference of Krulevitch et al. discloses the location of the optical analysis window and detection device with respect to specimen and analysis chamber (40) which is in communication with the specimen chamber.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 and 16-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 5,985,217 in view of Pourahmadi et al.(WO 99/33559). Claims 1-15 of U.S. Patent 5,985,217 encompass a microfabricated biopsy/genetic analysis instrument, comprising: a cutter section, a specimen chamber located adjacent said cutter section, a specimen treatment section located adjacent said specimen chamber.

While the claims disclose that the device includes microchannels for delivering chemicals for treating the specimen, claims 1 and 16 differ by reciting that the device includes a PCR reaction chamber section "that is integral with said specimen treatment section or abuts" the specimen treatment chamber.

The reference of Pourahmadi et al. discloses that it is known in the art to combine microfabricated sample preparation device, including tissue slicing or cutting with microfabricated analyte detection and/or microfabricated polynucleotide amplification. The reference of Pourahmadi et al. discloses a microfabricated biopsy and genetic analysis instrument that includes a cutter section and specimen chamber (103) located below the cutter section. See page 20, line 27, to page 21, line 10, which discloses that the opening of the specimen chamber (sample port, 103) can include a mesh that slices a tissue specimen. The instrument includes a specimen treatment section (including treatment chambers 107, 119, 122, 141) located adjacent the specimen chamber (103) and a PCR reaction chamber section that is integral or abuts the specimen treatment section. See page 12, lines 13-26, which discloses that the PCR reaction chamber (143) can be integral or separable relative to the sample treatment section of the instrument.

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ the tissue cutting device encompassed by the patented in place of the mesh material employed by the reference of Pourahmadi et al. for the known and expected result of providing an alternative means recognized in the art to achieve the same result, cutting or slicing a tissue sample prior to introduction into a microfluidic device while providing art recognized microfluidic structures for further processing and analysis of the tissue sample.

With respect to claim 2, see patented claim 2.

With respect to claims 3 and 4, see patented claim 7.

With respect to claims 5, the reference of Pourahmadi et al. discloses the use of microchannels (See Figure 2) to connect the sample chamber (103) with the PCR reaction chamber (143). Also the reference discloses the use of planar members, including glass, to form the device (See page 26, line 35, to page 27, line 28).

With respect to claims 16 and 19, see patented claims 4 and 6.

With respect to claim 17, the reference of Pourahmadi et al. discloses that the PCR reaction section (143) can be formed as a separate member or integral member (See page 12, lines 14-16).

With respect to claim 18, see patented claim 2 and note the reference of Pourahmadi et al. discloses that the PCR reaction chamber (143) includes a heater (See page 12, lines 13-26).

9. Claims 1-5 and 16-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,319,474 in view of Pourahmadi et al.(WO 99/33559). Claims 1-5 and 16-19 are obvious over claims 1-19

of patent '474 and the reference of Pourahmadi et al. for the same reasons as set forth with respect to the combination of Claims 1-15 of U.S. Patent '217 and Pourahmadi et al. set forth above.

Response to Arguments

10. With respect to the 35 USC 112, 2nd paragraph, rejections of record, Applicants' argue (See page 6 of the response filed 7/18/05) that removal of the terms "sections" and "regions" from the claims is sufficient to overcome the rejections of record.

In response, the Examiner maintains that the rejection is proper because the instant claims employ the transitional language "consisting", however, the metes and bounds of the claim cannot be clearly determined because it is not clear if the instant claims are limited solely to "a specimen treatment and analysis **chamber**" or additional structural elements that would define "a specimen treatment and analysis chamber" such as reagents and/or inlet ports for adding reagents, detectors, etc. The same holds true for the recited PCR reaction chamber. This claim language makes it difficult to compare the instant claims with the prior art. For example, if the prior art discloses a PCR chamber that includes a heater and heater controller, it is not clear if the instant claim limitations of a PCR chamber has been met in view of the instant claim language. Or is the Examiner required to explain why it would be obvious to remove the heater and associated controller from the PCR chamber of the prior art device.

11. With respect to the rejection of claims 1, 5, 6, 9-14 and 16-19 under 35 USC 102 over the reference of Pourahmadi et al., Applicants' amendments and associated comments (See pages 6-10 of the response dated 7/18/05) are persuasive to overcome the rejection of record.

12. With respect to the rejection of claims 2-4, 7, 8, 15 and 19 under 35 USC 103 over the combination of the references of Pourahmadi et al. and Krulevitch et al., Applicants argue (See pages 10-12 of the response filed 7/18/05) that the combination of the references is not proper for the following reasons:

i) The reference of Pourahmadi et al. does not disclose all of the instantly recited claim elements.

ii) The reference of Krulevitch et al. does not disclose all of the instantly recited claim elements.

iii) In view of arguments i) and ii) above, the combination of the references of Pourahmadi et al. and Krulevitch et al. would not result in the claimed invention.

iv) There is no motivation to combine the references of Pourahmadi et al. and Krulevitch et al.

In response to arguments i) and ii) above, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to argument iii) above, the Examiner maintains that the combination of the references as recited in the 35 USC 103 rejection of record meets the structure of the claimed device for the reasons specifically set forth in the rejection of record.

In response to argument iv) above, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case the Examiner is of the opinion that since the reference of Pourahmadi et al. discloses the use of a cutter device with a sample preparation and analysis device including PCR, one of ordinary skill in the art would have readily recognized the advantages of using the cutting device disclosed by the reference of Krulevitch et al.

Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kim can be reached on 571-272-1142. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

William H. Beisner
Primary Examiner
Art Unit 1744

WHB